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Commentary: Early-stage esophageal cancer: The tip of the iceberg

Thomas Boerner, MD, and Daniela Molena, MD

The introduction of organ-preserving endoscopic resection has brought a paradigm shift in the treatment of superficial esophageal cancer. For T1a tumors, endoscopic therapy has become the standard of care in many centers, as it is safe and feasible without compromising survival.¹ Enthusiasm for the procedure has increased its application for more-advanced cancers,² and although it would be ideal to preserve the esophagus in all such patients, endoscopic therapy might not be the best option—even when feasible—to cure disease. T1b tumors penetrating the deep submucosa are associated with a substantial risk of lymph node involvement,³ and at present, we lack tools to identify patients with residual disease after endoscopic therapy who would benefit from a more-invasive approach, such as esophagectomy, and/or patients with a high risk of recurrence likely to benefit from adjuvant treatment. We see (and treat) the tip of the iceberg without knowing the more dangerous and aggressive part lies underneath the surface. Until efficient ways to assess residual disease are available, we must rely on pathologic factors that help stratify the risk of nodal involvement, such as tumor size, histologic differentiation, lymphovascular invasion (LVI), and depth of invasion.

Wang and colleagues⁴ reviewed their experience assessing tumor extension to the ductal system of submucosal

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A retrospective study shows that ductal involvement of submucosal glands is a risk factor for recurrence in patients with early-stage esophageal squamous cell cancer undergoing curative-intended ESD.

glands in patients undergoing endoscopic submucosal resection (ESD) for superficial squamous carcinoma (N = 210). Their primary aim was to evaluate the clinical impact of ductal involvement (DI) on staging, recurrence, and survival. Presence of DI was observed in 37.1% of patients and, in addition to LVI, was associated with worse survival. In patients who underwent curative ESD (R0 resection and no deep submucosal invasion or LVI), DI was associated with a greater risk of local recurrence (12.7% vs 2.5%) and was associated with shorter recurrence-free survival (hazard ratio, 4.20; $P = .038$).

We commend the authors for their excellent work and thorough histologic assessment of DI. The study highlights the importance of accurate histologic staging in early-stage esophageal cancer and the unmet need for better stratification criteria in this patient population. Consideration of submucosal glands and their ducts is innovative and potentially adds new information to aid clinical decision-making. A high overall recurrence rate (37.7%) was observed in patients with DI after successful ESD, which suggests cancer cells may spread through the intraductal system of the esophageal glands, reaching a deeper depth of invasion than otherwise suspected and potentially leading to residual disease in the glands.

We must be careful, however, when drawing conclusions about the effect of DI. Even though DI was

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independently associated with risk of recurrence, the patient cohort was small, and studies have shown substantial interobserver variability in assessing pathologic risk factors. These findings need validation within larger-scale studies.

Future work should focus on innovative methods to identify patients with residual disease and risk of recurrence after endoscopic therapy. A promising approach might be to use liquid biomarkers, such as circulating tumor DNA, which has shown encouraging results for the detection of residual disease in advanced esophageal cancer after treatment.⁵ It is clear that defining the best therapy for patients with early-stage disease remains challenging and that we urgently need new navigation tools to prevent us from hitting the iceberg.

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Commentary: Endoscopic treatment is the key for superficial esophageal squamous cell neoplasia

Ke-Neng Chen, MD

Wang and colleagues¹ retrospectively reviewed 210 patients with superficial esophageal squamous cell neoplasia (SESCN) who were treated by endoscopic submucosal dissection (ESD) between 2009 and 2017. There were 185 patients who received curative ESD, namely, R0 resection, no deep submucosal invasion, and no lymphovascular invasion. The investigators found that ductal involvement was a

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Traditional esophagectomy should be selected carefully for superficial esophageal cancer. Thorough examinations and full multidisciplinary discussion should be performed to select appropriate patients.

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poor prognostic factor for patients with SESCEN treated by ESD. I strongly support ESD treatment for SESCEN.

A BRIEF HISTORY OF TREATMENT FOR EARLY ESOPHAGEAL CANCER

Traditional esophagectomy has a 100-year history, and it has been the principal treatment for superficial esophageal